AMENDMENTS TO THE SPECIFICATION

Please direct the Sequence Listing filed herewith into the application.

Please replace the paragraph beginning at line 12 on page 60 with the following paragraph:

Primer design

Based on the location of the reported most-far 5'-breakpoint and available nucleotide sequences from the *BCL1*-MTC region (GenBank accession number S77049), we designed a single *BCLl* primer (5'-GGATAAAGGCGAGGAGCATAA-3') (SEQ ID NO: 98) in the 472-bp region 5' of this breakpoint by using the primer design program OLIG06.2 relative to the consensus JH primer.

Please replace the paragraph beginning at line 19 on page 60 with the following paragraph:

Results of initial testing phase

Using the consensus JH-primer in combination with the single *BCL1*-MTC-primer on a small series of MCL (n=5) previously identified as positive with an in-house BCLI/JH-PCR using a similar consensus JH18-primer (18 nt) and 5'-GCACTGTCTGGATGCACCGC-3' (SEQ ID NO: 131) as *BCL1*-MTC-primer, we initially compared both assays in parallel. In contrast to the analysis of Ig/TCR gene rearrangements via GS and/or HD analysis, the *BCL1*-JH PCR products (as for *BCL2*-JH products) are identified via agarose gel electrophoresis using ethidium bromide staining only. The results on the five positive and two negative samples were identical except that the PCR products were significantly weaker. To evaluate whether we could increase the sensitivity of the PCR, we determined the effect of different concentrations of $MgCl_2$ and primers, and different temperatures in a Stratagene-Robocycler PCR-machine (all other PCR were done on ABI-480 or ABI-9700). Most intriguing was the variation due to small changes in $MgCl_2$ concentration. At 2.0 mM a weak nonspecific product of 550 bp became apparent whereas at 2.5 mM and higher this nonspecific product was very prominent in all DNAs including non-template DNA controls. At lower concentrations (less than 1.5 mM) no

nonspecific fragments were observed but the expected specific products were very weak. Hybridizations with a *BCL1*-MTC-internal oligo-probe (5'-ACCGAATATGCAGTGCAGC-3') (SEQ ID NO: 132) did not show hybridization to this 550 bp product. PCRs with each of the primers separately revealed that the 550 bp product could be generated by using the JH-consensus primer only. In some MCL cases, in addition to the PCR-products ranging from 150-350 bp (Figure l0), larger specific PCR-products might be apparent due to annealing of the consensus JH-primer to downstream JH5 and JH6 segments as described for *BCL2*/JH.[140] From the initial testing phase the most optimal PCR-conditions for the *BCL1*-MTC/JH-PCR were: annealing temperature of 60°C, 2.0 mM $MgCl_2$ and 10 pmol of each primer (for 35 PCR-cycles in the ABI 9700).

Please replace the paragraph beginning at line 15 on page 65 with the following paragraph:

In order to improve the sensitivity of the assay within this region we designed three further primers that spanned the 3'MBR sub-cluster region; 3'MBR2, 3'MBR3 and 3'MBR4 and combined them with 3'MBR1 and the consensus JH in an additional multiplex reaction; 3'MBR multiplex (Figure 11). This new approach confirmed that eight of the 32 cases were positive but missed the ninth case. The primers were then used individually and in this experiment 11 of the 32 cases were positive. The breakpoints were distributed as follows; 2/11 cases had a breakpoint present between primer 3'MBR1 and 3'MBR2, 3/11 cases between primers 3'MBR2 and 3'MBR3, 2/11 cases between primers 3'MBR3 and 3'MBR4 and the remaining four cases amplified using primer 3'MBR4 and were distributed 200-1000bp 3' of this primer. In this series of cases there were three false negative results using the 3'MBR multiplex. One of the cases was a true false negative where the break occurred in the middle of the 3'MBR, in proximity to an Alu repeat sequence. The translocation was detected using the 3'MBR3 primer when used in isolation and a product of 450 bp was generated suggesting a reduced sensitivity of the multiplex. The remaining two false negative cases generated products larger than 1000bp with the 3'MBR4 primer, placing them in the far 3'MBR not fully covered by this approach. Further improvement in the sensitivity of the 3'MBR assay has been achieved following the general testing phase of this study. Substituting primer 3'MBR3 with a new downstream primer

5'-GGTGACAGAGCAAAACATGAACA-3' (SEQ ID NO: 109) (see Figure 11A) significantly improved both the sensitivity and specificity of the 3'MBR assay.